REMARKS / ARGUMENTS

In response to the Office Action of August 18, 2009, Applicants have canceled claims 7, 9, 10 and 21, which when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of claim 8 based on the remarks below is respectfully requested.

Claims 9, 10 and 21 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with both the written description and enablement requirements. In response to the rejection, and in order to advance prosecution of this application, claims 9, 10, and 21 have been canceled without prejudice. Applicants reserve the right to file one or more continuation applications directed to the subject matter of the canceled claims.

Claims 10 and 21 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 3-5 of copending Application No. 12/075,159. As discussed fully above, claims 10 and 21 have been canceled from the application, rendering the provisional rejection moot.

Claims 7 and 9 have been rejected under 35 U.S.C. 102(b) as allegedly anticipated by Gault et al. (*J. Neurochem.* 1998; 70:1907-1915). In order to advance prosecution of this application, claims 7 and 9 have been cancelled without prejudice. Applicants reserve the right to file a continuation application directed to the subject matter of canceled claims 7 and 9.

Claim 8 has been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over WO 96/10637 to LeBourdelles et al. in view of Smith et al. (Abstract from the a11th

congress of the International Society for Biomedical Research on alcoholism, *Alcoholism Clinical Exp Res.* 2002 May; 26(5 Suppl):16A, Abstract #65.

LeBourdelles et al. is relied upon for allegedly teaching methods of stably co-transfecting eukaryotic cell lines to express a $GABA_A$ receptor, and methods of using such cell lines in screening and design of drugs which act on the $GABA_A$ receptor. The reference is also relied upon for allegedly teaching that the host cell should be transfected with at least three expression vectors, each harboring cDNAs encoding an α_4, β, or δ $GABA_A$ receptor subunit. LeBourdelles et al. has also been cited for allegedly teaching that it is necessary to incorporate the α_4 subunit, at least one β subunit, and the δ subunit into the cell line in order to produce the required receptor, although the choice of the receptor subunit combination can vary according to the type of activity or selectivity which is being screened.

On page 14 of the office action, the examiner summarizes the alleged teaching of LeBourdelles et al. as a method for screening for a drug which acts upon the $GABA_A$ receptor by: (a) expressing $\alpha_4\beta_2\delta$ $GABA_A$ receptors in eukaryotic cells; (b) applying a drug to the eukaryotic cells of (a); and determining whether he drug modulates the $\alpha_4\beta_2\delta$ $GABA_A$ receptor in *some manner* to thereby identify a drug which acts upon the $\alpha_4\beta_2\delta$ $GABA_A$ receptor. The Examiner readily admits that LeBourdelles et al. does not teach measuring the expression level of the δ subunit of the $GABA_A$ receptor for drug screening.

In order to fill the gap of teaching left by LeBourdelles et al., Smith et al. has been cited for allegedly teaching modulation of $\alpha_4\beta_2\delta$ $GABA_A$ receptors following withdrawal from chronically administered progesterone in female rats. Smith et al. is

also relied upon for teaching that in pharmacological studies, $\alpha_4\beta_2\delta$ $GABA_A$ receptor responses were assessed by measuring the level of α_4 and δ subunit expression and also by voltage-clamp recordings. Smith et al. has also been cited for allegedly correlating the *in vitro* data to *in vivo* behavioral responses in the animals, noting that progesterone withdrawal leads to greater sensitivity to low doses of ethanol, presumably through the enhanced expression of $\alpha_4\beta_2\delta$ $GABA_A$ receptors following withdrawal.

According to the Examiner, it would have been obvious to one of skill in the art at the time the invention was made to utilize the types of measurements taught by Smith et al. such as measuring the expression of α_4 and β_2 subunits in the screening method taught by LeBourdelles et al. so as to arrive at the claimed invention.

Applicants respectfully traverse the rejection of claim 8 as allegedly obvious for the following reasons. There is no teaching, hint, motivation or suggestion in the combination of cited references that screening for a drug that decreases expression of the $\alpha_4\beta_2\delta$ $GABA_A$ receptor could be performed by measuring the level of only the δ subunit in eukaryotic cells expressing $\alpha_4\beta_2\delta$ $GABA_A$ receptors. This teaching first appears in Applicants' disclosure at page 28, where a discussion is provided that functional $GABA_A$ receptors can assemble from some α and β subunits, in the absence of a δ subunit. Measuring the δ subunit in eukaryotic cells ensures that any $GABA_A$ receptor though functioning, actually contains the δ subunit.

It is respectfully submitted that LeBourdelles et al. teach various combinations of $GABA_A$ receptor subunits derived from cultures of transfected eukaryotic cells and that the cells lines and membrane preparations therefrom "have utility in screening and design of drugs which act upon the $GABA_A$ receptor". Such methods, however, are

never fully disclosed. There is certainly no hint, suggestion, or motivation for the presently claimed invention where a decrease in the expression of the δ subunit is measured and used to identify a drug which decreases expression of the $\alpha_4\beta_2\delta$ subunit of $GABA_A$ receptor.

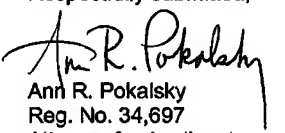
The Smith et al. reference assesses GABA-modulatory effects of ethanol on a variety of $GABA_A$ receptor subunit combinations. The authors found increased coexpression of α_4 and δ subunits following withdrawal from progesterone, suggesting that an increased expression of $\alpha_4\beta_2\delta$ receptors following withdrawal from progesterone enhances the GABA potentiating effects of low doses of ethanol. There is nothing in Smith et al. that would lead one to the presently claimed invention of screening for a drug with decreases expression of the $\alpha_4\beta_2\delta$ $GABA_A$ receptor via measuring a decrease in the δ subunit of a $GABA_A$ receptor.

It is respectfully submitted therefore, that the propositions of law handed down in *KSR Int'l. Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742 , 8 USPQ2d 1385, 1396 (2007), which the Examiner has used to support the rejection claim 8, do not apply in this case. Applicants' position is predicated on the failure of the cited references to suggest measuring a decrease in the δ subunit of a $GABA_A$ receptor as either a technique that has been used to improve one device (in this case, one methodology), or as a solution based on design need or market pressure. The suggestion to measure a decrease in the δ subunit of a $GABA_A$ receptor as a technique in a drug screening assay and the design need to ensure that functional $GABA_A$ receptors comprise the δ subunit, first appears in Applicants' disclosure. The rejection of claim 8 as allegedly obvious over LeBourdelles et al. in view of Smith et al., is therefore based on the benefit of hindsight

reconstruction, still prohibited under *KSR*. Withdrawal of the rejection of claim 8 under 35 U.S.C. §103(a) is therefore respectfully requested.

Accordingly, in view of the foregoing remarks and amendments, the present application is believed to be in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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